Favorable reconsideration in light of the amendments and remarks which follow is respectfully requested.

1. 35 USC §112 Rejection

Claims 22-33 and 49-90 have been objected to under 35 U.S.C. §112, second paragraph, as being indefinite. The Office states that:

> Claim 22 is a method of preparation claim and therefore should recite method step leading to the formation of transfersome. Step a recites selecting the lipid components and step b recites suspending the transfersome. There is no step in the claim as to how the transfersomes are formed. This is critical in view of applicant's assertion that transfersomes are different from liposomes.

Applicant has amended claim 22 to include a method step leading to the formation of transfersome.

The Office further states that "The distinction between the pharmaceutically acceptable medium in step a and the solubilizing agents in step c is unclear."

The term "pharmaceutically acceptable suspending medium" is described on p. 6, last paragraph, p. 7, second paragraph and p. 21, second paragraph. As set out, the pharmaceutically acceptable suspending medium is the liquid medium in which the transfersomes are formed.

The term "solubilizing agent" no longer appears in the amended claims. Applicant respectfully submits that the term "solubilizing agent", as originally contained in the claims, refers to the more soluble component of the two amphiphilic lipid components. This amphiphilic lipid component is called a "solubilizing agent" because it represents the component acting as the destabilizing component due to its better solubility in the pharmaceutically acceptable suspending medium. The less soluble component of the two amphiphilic lipid components, on

the other hand, acts as the structure building substance. Thus, as requested by the Examiner, to more clearly distinguish between the "pharmaceutically acceptable suspending medium" and the "solubilizing agent", Applicant has replaced the term "solubilizing agent" with reference to the more soluble component of the two amphiphilic lipid components.

The Office further states that "Also unclear as to how one can adjust the amphiphilic lipid components once the transfersomes are formed as recited in step d."

Claim 22 has been amended to clarify formation of the transfersomes and adjustment of the amphiphilic lipid components.

The Office further states that:

> It is unclear as to how one can determine the permeability through skin by filtration or other methods recited in claim 24. What is being conveyed by "under pressure"? What is subjected to under pressure? "Fine" in fine pored filter is indefinite; fine is a relative term.

"Permeability" refers to the perviousness of the materials to be permeated, whereas "permeation" refers to the penetration of this material, i.e., "permeation capability", which is actually mentioned in claim 24, describes the ability of the transfersomes to permeate through barriers like the skin. Generally, the methods cited in claim 24 are useful for determining the permeation capability of the transfersomes of the present invention through the skin by means of testing their stability under high stress. Example of such stress may be filtration of the transfersomes through a fine-pored filter under pressure. The results of these tests are fully transferable to biological systems. Therefore, if transfersomes pass this test, they also have sufficient stability to pass through the pores of the skin (see Examples 8-17), i.e. they are capable of permeating through such barriers without bursting.

Further means of stress may be controlled mechanical blending, shearing or comminuting. All of these methods exert high stress on the stability of the transfersomes. Therefore, of they stand this stress, it can be concluded that they are stable enough to stand the permeation stress as well.

Regarding the use of the term "fine" in fine pored filter, Applicant respectfully submits that "fine pores" is a common term in the art used to describe pores with an average diameter of about 1 to 200 nm. Representative fine-pored filters, as understood by those skilled in the art, may include such filters as shown in Figures 6-8, which have a pore size of about 30 to 100 nm.

Accordingly, Applicant respectfully submits that the term "fine" in fine-pored filters is not indefinite.

The Office further states that:

> 'other mechanical comminuting effects' in claim 25 is indefinite; other is not a positive expression; specific methods should be recited.

Applicant has amended claim 25 accordingly to delete reference to "other".

The Office further states that:

> The distinction between the polar liquid recited in claim 26, pharmaceutically acceptable medium and the solubilizing agents is recited in claim 22 is unclear.

The distinction between pharmaceuticaly acceptable medium and solubilizing agents recited in claim 22 is set out above.

The "polar liquid" of claim 26 is equivalent to the pharmaceuticaly acceptable medium set out in claim 22. Accordingly, the term "polar liquid" has been replaced with "polar pharmaceuticaly acceptable medium".

The Office further states:

> What is meant by 'optionally brought into solution' as recited in claim 28? If they are brought into solution, then how are transfersomes formed? Similar is the case with claim 29.

Claim 28 reads as follows:

> 28. The method of claim 22, wherein said amphiphilic components and a hydrophilic substance are mixed separately with an active ingredient and optionally brought into solution, and then combined to form transfersomes.

Applicant respectfully submits that claim 28 describes the preparation of transfersomes by separately producing:

1. a mixture of the amphiphilic components and the active ingredient, and
2. a mixture of a hydrophilic substance and the active ingredient.

As set out, 1. and 2. may optionally be brought into solution at this time. Subsequently, the mixtures are combined (whether is solution or not), whereby transfersome formation is induced.

Claim 29 reads as follows:

> 29. The method of claim 22, wherein said amphiphilic components, either as such or dissolved in a physiologically compatible solvent or a dissolving intermediary, which is miscible with a polar liquid or liquids, are combined with a polar solution.

Applicant respectfully submits that claim 29 describes the following:

1. a polar pharmaceutically acceptable medium is provided,
2. the amphiphilic components are mixed together together:
    a. without being dissolved or suspended in a suitable medium, or
    b. dissolved in a physiological acceptable solvent or solutizer, which must be miscible with polar liquids,
3. the amphiphilic components (dissolved or not) are combined with the polar pharmaceutically acceptable medium, which leads to the formation of transfersomes.

Applicant points out that even if the components are dissolved, they can form transfersomes upon combination. This is namely because the components, as such, are soluble, whereas formation of the transfersomes only occurs by the addition of the polar medium, which induces the transfersome formation. This is a typical phenomenon in (bio)chemistry wherein two liquids are combined, which together form a solid, or memberanes, etc.

The Office further states:

> What is meant by 'rubbing' in claim 30? The terms, 'low' and 'high' are relative terms. The temperature units should be recited for 'heating' and cooling' in claim 30.

Applicant has replaced the term "rubbing" with "grinding" or triturating". Use of the term "rubbing" was due to a translational error.

Regarding the terms "low pressure" and "high pressure", there is no general definition of high pressure and low pressure filtration due to the dependency of the minimum required pressure on system properties (Darcy- and Young-Law). The application of the pressure to be applied is dependent, inter alia, from the pore size of the filters, the diameter of the filter, etc. Thus, the terms have been replaced with "filtration under pressure".

The terms "heating" and "cooling", likewise have been deleted accordingly. In accordance with the present invention, as set out in amended claim 30, heating and cooling are applied until transfersome formation begins.

The Office further states "What is prepared from a concentrate as recited in claim 33?"

Applicant respectfully submits that a typographical error was made wherein the words "enveloped droplets" were omitted from claim 33. Thus, claim 33 has been amended accordingly.

The Office further states "what is meant by 'reference particle' in claim 50 (and 49)? This term lacks antecedent basis in claim 23."

Claim 23 was previously amended to replace "reference particles" with "water". Thus, claims 49 and 50 have, likewise, been amended.

The Office further states that "Claim 52 is not further limiting claim 31 in terms of pore size."

Applicant respectfully disagrees. Claim 31 reads as follows:

31. The method of claim 22, wherein the formation of the transfersomes is brought about by filtration and the filter material used in said filtration has a pore size of **0.01 μm to 0.8 μm**.

Claim 52 reads as follows:

32. The method of claim 31, wherein the formation of the filter material has a pore size of **0.08 μm to 0.15 μm**.

The Office further states that:

> It is unclear whether the claim 53 is a treatment claim or transport claim. If it is a treatment claim, the condition of the mammal to be treated should be recited.

Applicant respectfully submits that claim 53 is directed to both a method of transport and a method of treatment of a mammal. In the case where claim 53 is directed to a method of treatment of a mammal, the condition of the mammal to be treated depends on which active ingredient is used.

As indicated in claim 84, various active agents in accordance with the present invention may be selected from the group consisting of: an adrenocorticostatic agent, a β-adrenolytic agent, an androgen, and antiandrogen, an anti-parasitic, an anabolic, an anesthetic, an non-narcotic analgesic, an analeptic, an anti-allergic, an anti-arrhythmic, an anti-arteriosclerosis, an anti-asthmatic, a bronchospasmolytic agent, an antibiotic, an anti-depressive agent, an anti-psychotic agent, and anti-diabetic agent, an antidote, an anti-emetic, and anti-epileptic, an anti-fibrinolytic, and anti-convulsive agent, an anti-cholinergic agent, an enzyme, a coenzyme, a coenzyme inhibitor, an antihistamine, an antihypertensive drug, a biological activity inhibitor, an antihypotensive agent, an anticoagulant, an anto-mycotic, an antimyasthenic agent, an active ingredient against Parkinson's disease, an active ingredient against Alzheimer's disease, an anti-phlogistic, an anti-pyretic, an anti-rheumatic agent, an antiseptic, a respiratory analeptic, a respiratory stimulating agent, a broncholytic, a cardiotonic agent, a chemotherapeutic agent, a coronary dilator, a cytostatic agent, a diuretic, a ganglion blocker, a glucorcoticoid, a therapeutic agent for influenza, a hemostatic agent, a hypnotic agent, an immunoglobulin, a bioactive carbohydrate, a contraceptive, a migraine agent, a mineral corticoid, a morphine antagonist, a muscle relaxant, a narcotic, a neural therapeutic agent, a CNS therapeutic agent, a nucleotide, a polynucleotide, a neuroleptic agent, a neuron transmitter, a neuron transmitter antagonist, a peptide, a peptide derivative, a ophthalmic agent, a para-sympathicomimetic or para-sympathicolytic agent, a protein, a protein derivative, a psoriasis/neurodermatitis agent, a mydriatic agent, a mood elevator, a rhinological agent, a soporific, a soporific antagonist, a

sedative, a spasmolytic, a tuberculosis agent, a urological agent, a vasoconstrictor, a vasodilator, a virostatic agent, a wound-healing agent, and a non-steroidal antiinflammatory agent.

Thus, claim 53 has been amended to include the various types of conditions which are treatable by these active agents.

The Office further states:

> What is being conveyed by 'more soluble amphiphilic component is an active ingredient' as recited in claim 68? According to the parent claim 53, the active ingredient is separate from the two amphiphilic lipids.

Applicant respectfully submits that the active agent may be identical with the more soluble amphiphilic substance. Thus, for clarification, claim 53 has been amended accordingly.

The Office further states that

> Claim 72 recites a glyceride, a steroid and a sterol as amphiphilic lipid components. It is unclear how these can be considered as amphiphilic. What is meant by 'half protonated liquid fatty acid'?

Applicant respectfully submits that the term "amphiphilic", desfines molecules having both hydrophilic and lipophilic properties. The cited compounds clearly are amphiphilic substances. All of the examples given in the description on p.15, e.g., compounds like estradiol, or cholesterol have both hydrophilic and lipophilic groups, and, therefore, are amphiphilic. The same applies to glycerides.

Regarding the term "half-protonated liquid fatty acid", Applicant submits that a "half-protonated" fatty acid describes the state in which 50 % of the free fatty acids are protonated, and the other 50% are unprotonated.

The Office further states that:

> Claim 84 recites numerous active agents and the meaning of some of which is unclear. For example, 'a sleeping draft', 'a sleeping draft antagonist', 'bioactive carbohydrate', 'mineral corticoid', 'a biological activity inhibitor', 'coenzyme inhibitor' to name a few. Applicants should go through the list carefully and submit evidence to show that these are known terms. Furthermore, the claim recites, generic terms in terms of anti-disease agents and some specific compounds. There is considerable overlapping of the compounds.

Applicant has amended the terminology , "sleeping draft" and "sleeping draft antagonist" to "soporific" and soporific antagonist". Applicant respectfully submits that the terms in claim 84 referring to the numerous active agents are commonly known to those skilled in the art and, for example, are explained in standard pharmaceutical encyclopedias. For example, "bioactive carbohydrate" is a common term defining biologically active carbohydrates, e.g. trehalose (a water-replacing di-hexose), muramic acid and cord factor (immuno-modulating sugars), and sialyl lactose (found in human breast milk); a list of interesting corresponding carbohydrates can be found in a recent publication titled "Bioactive Carbohydrate Polymers, Ed.: Berit S. Paulsen Binding, Kluwer Academic Publishers, 2000. "Mineral corticoid" is a common term for a group of endogenic corticosteroids controlling the mineral metabolism, e.g. cortexolone, cortexol, and aldosterol. "Biological activity inhibitor" is a commonly used term for an antagonist of biological action of any given target molecule. "Coenzyme inhibitors" are substances inhibiting the activity of coenzymes.

The Office further states: "What is being conveyed by 'growth regulating substance' as recited in claim 87?"

Applicant respectfully submits that "growth regulating substance" is a term known to those skilled in the art. The term defines substances, the application of which can modify the metabolism of plants, and animals. Growth regulating substances are mainly used in plants in order to promote or inhibit growth, control the ripeness of fruit, etc.

The Office further states that "'Active ingredient' in claim 84, 85 and 87-89 lacks antecedent basis in claim 53."

Applicants respectfully submit that use of the term "active ingredient" was a typographical error. Rather, the term should have been "active agent", which appears in claim 53. Accordingly, Applicants have amended the term "active ingredient" to "active agent" in claims 84, 85 and 87-89.

The Office further states that "It is unclear what the allurement allures as recited in claim 89."

Applicants respectfully submit that "allurement" is a common term for substances which lure specific organisms, such as, e.g., insects. Typical examples are pheromones.

In view thereof, reconsideration and withdrawal of the rejection are respectfully requested.

2. 35 U.S.C. §102 Rejections

Claims 22-33 and 49-90 have been rejected under 35 U.S.C. §102 (b) as being anticipated by EP 0 475 160. The Office states that:

> EP discloses instant composition containing a drug, and amphiphilic lipid and a surfactant in instant amounts and a method of preparation.

Applicants respectfully traverse this rejection.

The present invention describes transfersomes, methods of delivering transfersomes through the skin or mucous membrane of a mammal and methods of using transfersomes to treat a variety of conditions in mammals.

Transfersomes are differ from liposomes in a number of ways. Liposomes are relatively firm spherical objects formed by one or several concentrical lipid bilayers having an aqueous interior. These liposomes are prepared, e.g., by mechanical dispersion of amphiphilic phospholipids like phosphatidyl choline in aqueous media. Liposomes typically have a relatively inflexible and rigid membrane-like sheath, and, therefore, are firm, i.e. they are not deformable without bursting. Thus, liposomal preparations for dermal application are generally only suitable for the administration of agents to the uppermost layer of the skin. Thus, such preparations are deposited on or in the uppermost layer of the skin, which consists of dead cells. As time passes, the liposomes disintegrate in this layer, releasing their liquid contents. Some of the membrane material may then act as a skin softener. This is a slow and very inefficient process of transdermal agent transport in solution, wherein the intact liposomes act just as a reservoir for the solution. Transdermal administration of agents, i.e. a penetration into and through the permeability barrier of the skin by such liposomes or liposomal preparations is not possible. The pores of the skin are not sufficiently wide for the permeation of the rigid spherical one- or multi-layer liposomes into and through the lower skin layers due to their lack of flexibility. Application of external pressure to the liposomes would lead to the destruction of the rigid

membrane-like sheath. Thus, liposomes act merely as a reservoir of the agent solution on the skin.

The transfersomal preparations of the present invention provide new preparations that allow the transport of active agents through barriers and constrictions, e.g. the skin. These transfersomes behave completely different than liposomes behave. Trensfersomes are vesicles having a membrane-like sheath comprising amphiphilic substances surrounding liquid droplets. However, in contrast to liposomes, transfersomes are highly flexible vesicles having a highly deformable membrane-like sheath. Due to their flexibility, transfersomes are capable of penetrating the skin intact and, consequently, are capable of transporting agents through the skin. Unlike hard spheres, transfersomes can assume a highly elongated shape and, thus, can penetrate into the outer skin pores, which are much wider than the inner skin pores. They can then widen the pores and, thus, work their way into the skin and through the inner skin pores. The driving force is provided by the moisture gradient across the skin. The transfersomes do not disintegrate while passing through the skin. No known liposome can perform this transdermal permeation.

There are various types of transfersomes varying in the number and kind of different amphiphilic and surfactant membrane components. The transfersomes of the present invention may include a liquid droplet surrounded by a membrane-like sheath of one or more layers of amphiphilic carrier substance. The carrier substance comprises at least two (physio)chemically different amphiphilic components which differ in their solubility in the pharmaceutically acceptable medium of the preparations by a factor of at least 10. The combination of more soluble and less soluble amphiphilic substances, provides deformability of the transfersomes. The composition of the sheath formed by the less soluble substance is softened by the presence of the more soluble substance, such that the vesicles get more and more flexible. The flexibility provides a high deformability and, thus, provides the permeation capability of the transfersomes through barriers and constrictions, e.g. the skin.

Claim 53 is directed to a method of treatment of a mammal with a preparation for the transport of active agents through the skin or mucous membrane of the mammal, in the form of liquid droplets, which can be suspended in a liquid medium, and which are provided with a membrane-like sheath of one or a few layers of amphiphilic carrier substance, the carrier substance comprising at least two physico-chemically different components.

Claim 22 is directed to a method for producing such preparations.

The preparations of the present invention are characterized in that: (1) at least two components are provided which differ in their solubility in the suspension medium by a factor of at least 10; and (2) the content of solubilizing components is less than 0,1 mol-% based on the content of these substances at which the solubilization point is reached; or (3) a solubilization point cannot be reached at all in this overall composition.

The "transfersomes" of EP 0 475 160 exhibit a clear solubilization point. On p. 3,l. 48 - 52, and in claim 1, preparations are disclosed, wherein the concentration range for the components with different solubility is between 0,1 and 99 mol-% of the concentration needed to solubilize the original lipid bilayer. Most frequently, optimum additive concentrations are between 10 and 60 % of the solubilization concentration. Also, figures 1, 3, 5, 6, 8, and 9 of the prior art, clearly show that all of the tested "transfersome" preparations have a solubilization point.

In contrast, claims 22 and 53 of the present invention teach preparations having a content of solubilizing components less than 0,1 mol-% based on the content of such substances at which the solubilization point is reached (for the case that there is a point of solubilization).

Furthermore, claims 22 and 53 of the present invention also include preparations wherein no solubilization point can be reached at all, which are not described or otherwise suggested by the references.

For example, Figure 1 of the present invention shows the decrease in the permeation resistance at a barrier as a function of the concentration of edge-active substance with respect to the approach to the solubilization point for "transfersomes" described in the state of the art, particularly those described is EP 0 475 160. Figure 2 of the present invention shows the decrease in the permeation resistance at a barrier as a function of the polar substance concentration with respect to the approach to a theoretical solubilization point, which cannot be reached in practice. In such rarer systems, there is no concentration that can be practically made at and above which solubilization occurs. The vesicle can always be formed. It is clear from Figure 2 that for the component system of the transfersomes described by the present invention, there is no solubilization point or the solubilization point is far away the point at which the maximum permeation capability is reached.

Thus, the reference does not deal with preparations as characterized by claims 22 and 53 of the invention. Furthermore, the reference is only directed to a lipid mixture comprising phosphatidyl choline and cholate with a concentration dependent solubilization point corresponding to an intro membrane lipid/detergent ratio around 1.

As provided in MPEP-2131, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Or stated another way, "The identical invention must be shown in as complete detail as is contained in the ... claims." *Richardson v Suziki Motor Co.*, 868 F.2d 1226, 9 USPQ 2d. 1913, 1920 (Fed. Cir. 1989). Although identical terminology is not required, the elements must be arranged as required by the claim. *In re Bond*, 15 USPQ2d 1566 (Fed. Cir. 1990).

It is clear from the foregoing remarks that claims 22 and 53 are not anticipated by the EP 0 475 160 reference. Claims 23-33, 49-52 and 54-90 depend from claims 22 and 53 and, likewise, are not anticipated by the EP 0 475 160 reference.

3. 35 U.S.C. §103 Rejections

Claims 22-33 and 49-90 have been rejected under 35 U.S.C. §103(a) as being unpatentable over the EP 0 475 160 reference. The Office states:

> As pointed out above, EP teaches a composition contianing a drug, an amphiphilic lipod and a surfactant in instant amounts and a method of preparation. It is unclear whether the reference teaches all the instant functional parameters. In case they are different, in the absence of showing the criticality, they are deemed to be parameters manipulable by an artisan to obtain the best possible results.

Applicant respectfully traverses this rejection.

As set out above, the reference merely describes preparations having a clearly defined solubilization point, and, on the other hand expressly teaches that the solubilizing components have to be present in a concentration of more than 0.1, mol-% of the content of these substances at which the solubiliwtion point is reached.

The present invention, as claimed in claims 22 and 53, expressly teaches the use of less than 0.1 mol-% of solubilizing components.

It is well-known that to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference(s) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of

success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2143.

As set out above, the EP 0 475 160 reference does not teach or suggest all of the claim limitations. Namely, the EP 0 475 160 reference fails to teach or suggest (a) the use of less than 0.1 mol-% of solubilizing components. Further, there is absolutely no teaching or suggestion in the prior art to modify the reference to meet the claim limitations. Rather, reference clearly teaches away from such modification. The prior art expressly teaches to use more than 0.1 mol-%, and, rather to approach the upper end of the solubilization concentration. Further, there is no suggestion that providing concentrations of less than 0.1 mol-% of the solubilizing components would lead to improved characteristics, e.g. an improved permeability of the resulting transfersome preparations. Still further, there is no teachjng or suggestion to modify the reference to provide preparations having no point of solubilization at all.

Thus, it is clear that claims 22 and 53 are patentable over the EP 0 475 160 reference. Claims 23-33, 49-52 and 54-90 depend from claims 22 and 53 and, likewise, are patentable over the EP 0 475 160 reference.

CONCLUSION

Reconsideration and allowance of claims 22-33 and 49-90 is respectfully requested in view of the foregoing discussion. This case is believed to be in condition for immediate allowance. Applicant respectfully requests early consideration and allowance of the subject application.

Should the Examiner wish to discuss any of the amendments and/or remarks made herein, the undersigned attorney would appreciate the opportunity to do so.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE IN CLAIMS

Please note that additions to the claims are shown underlined and deletions are shown in brackets.

22. A method for producing a preparation for transporting at least one active ingredient through the skin or mucous membrane of a mammal comprising:

a. selecting [at least two] a first amphiphilic lipid component[s]; and

b. selecting a second amphiphilic lipid component and selecting at least one active ingredient; or

c. selecting an amphiphilic active ingredient to form a second amphiphilic lipid component, and optionally selecting one or more further active ingredients;

d. said first and second amphiphilic lipid components being selected so that the [which differ in their] solubility of the second amphiphilic lipid component in a pharmaceutically acceptable suspending medium is at least ten times greater than the solubility of the first amphiphilic lipid component in said medium [by a factor of at least 10];

[b. suspending transfersomes containing said at least two amphiphilic lipid components in said pharmaceutically acceptable medium for application onto the skin or mucous membrane,]

d. adapting the composition or concentration of the preparation for transport through skin or mucous membrane, by adjusting the content of the more soluble component to less than 0.1 mole percent of the content of the first and second amphiphilic lipid components at which the enveloped droplets solubilize, if there is a solubilizing point; and

f. adjusting the content of amphiphilic lipid components, such that the ratio of the permeation capability relative to reference particles which are much smaller than the constrictions of the barrier, for example water, is between 10^{-5} and 1, especially between 10^{-2} and 1;

g. producing a transfersome suspension by means of applying energy to the mixture of said amphiphilic lipid components including at least one active ingredient, said transfersomes comprising liquid droplets encompassed within a sheath comprising said at least two amphiphilic lipid components, said amphiphilic lipid components being selected such that said transfersomes are capable of undergoing sufficient deformation to pass through said skin or mucous membrane without being solubilized, said active ingredient being contained in said liquid droplets, or in said sheath, or in both said liquid droplets and said sheath

[c. including one or more solubilizing components to provide adequate deformability to said transfersomes to pass through said skin or mucous membrane without being solubilized, if necessary, such that the content of solubilizing components is less than 0.1 mole percent, based on the content of said amphiphilic lipid components, at which the solubilizing point of the enveloped droplets is reached; and

e. adjusting the content of amphiphilic lipid components such that the ability of the transfersomes to permeate through said skin or mucous membrane is from about 0.001% to about 0.1% of the permeability of water].

24. The method of claim 22 wherein [the] stability and permeation capability [is] are determined by filtration[,] under pressure[,] through a fine-pored filter or by controlled mechanical whirling up, shearing or comminuting.

25. The method of claim 22, wherein [said transfersomes are produced by a method selected from the group consisting of filtration, treatment with ultrasound, stirring, shaking and other] the stability and permeation capability is determined by mechanical comminuting effects.

26. The method of claim 22 wherein the transfersome preparation is produced from at least to amphiphilic components of different polarity, at least one polar [liquid] pharmaceuticaly acceptable medium and at least one active ingredient.

27. The method of claim 22, wherein said amphiphilic component(s) comprises or contains the active ingredient, and said transfersomes are formed from at least two amphiphilic components of different polarity and at least one polar [liquid] pharmaceuticaly acceptable medium.

28. The method of claim 22 wherein said amphiphilic components and a hydrophilic substance are mixed separately with an active ingredient and optionally brought into solution and then combined to form transfersomes by supplying mechanical energy.

29. The method of claim 22 wherein said amphiphilic components, either as such or dissolved in a physiologically compatible solvent or [a dissolving intermediary amphiphilic components] or solutizer, which is miscible with a polar liquid or liquids, are combined with a polar pharmaceuticaly acceptable medium [solution].

30. The method of claim 22, wherein said transfersomes are formed by a method selected from the group consisting of stirring; evaporation from a reverse phase; an injection method; a dialysis method; electrical stressing; thermal stressing; a mechanical stressing selected from the group consisting of shaking, stirring, homogenizing, ultrasonicating, [rubbing] grinding or triturating, freezing, thawing, heating [,] and cooling until transfersome formation; [high pressure filtration;]and [low pressure] filtration under pressure.

33. The method of claim 22, wherein shortly before use, the enveloped droplets are prepared from a concentrate [or] of lyophilisate.

49. The method of claim 23, wherein the permeation relative to [reference particles] water is between 10^{-4} and 1.

50. The method of claim 23, wherein the permeation relative to [reference particles] water is between 10^{-2} and 1.

53. A method of treatment of a mammal in need thereof [with a preparation for the transport of at least one active agent through the skin or mucous membrane of the mammal], the method comprising administering to the skin or mucous membrane of the mammal [the] a preparation for the transport of at least one active agent through the skin or mucous membrane of the mammal, the preparation comprising:

transfersomes suspended in a pharmaceutically acceptable medium for application onto the skin or mucous membrane of a mammal, said transfersomes comprising:

liquid droplets encompassed within a sheath, said sheath comprising:

a first amphiphilic lipid component, a second amphiphilic lipid component and at least one active agent, or

a first amphiphilic lipid component, a second amphiphilic lipid component comprising an amphiphilic active agent and, optionally, one or more further active agents,

wherein said first and second amphiphilic lipid components differ in their solubility in said pharmaceutically acceptable medium by a factor of at least 10, said first and second amphiphilic lipid components being selected such that said transfersomes are capable of undergoing sufficient deformation to pass through said skin or mucous membrane without being solubilized, said active agent(s) being contained in said liquid droplets, or in said sheath, or in both said liquid droplets and said sheath, or being identical to the more soluble amphiphilic lipid component .

84. The method of claim 53, wherein the active [ingredient] agent is selected from the group consisting of an adrenocorticostatic agent, a β-adrenolytic agent, an androgen, and antiandrogen, an anti-parasitic, an anabolic, an anesthetic, an non-narcotic analgesic, an

analeptic, an anti-allergic, an anti-arrhythmic, an anti-arteriosclerosis, an anti-asthmatic, a bronchospasmolytic agent, an antibiotic, an anti-depressive agent, an anti-psychotic agent, and anti-diabetic agent, an antidote, an anti-emetic, and anti-epileptic, an anti-fibrinolytic, and anti-convulsive agent, an anti-cholinergic agent, an enzyme, a coenzyme, a coenzyme inhibitor, an antihistamine, an antihypertensive drug, a biological activity inhibitor, an antihypotensive agent, an anticoagulant, an anto-mycotic, an antimyasthenic agent, an active ingredient against Parkinson's disease, an active ingredient against Alzheimer's disease, an anti-phlogistic, an anti-pyretic, an anti-rheumatic agent, an antiseptic, a respiratory analeptic, a respiratory stimulating agent, a broncholytic, a cardiotonic agent, a chemotherapeutic agent, a coronary dilator, a cytostatic agent, a diuretic, a ganglion blocker, a glucorcoticoid, a therapeutic agent for influenza, a hemostatic agent, a hypnotic agent, an immunoglobulin, a bioactive carbohydrate, a contraceptive, a migraine agent, a mineral corticoid, a morphine antagonist, a muscle relaxant, a narcotic, a neural therapeutic agent, a CNS therapeutic agent, a nucleotide, a polynucleotide, a neuroleptic agent, a neuron transmitter, a neuron transmitter antagonist, a peptide, a peptide derivative, a ophthalmic agent, a para-sympathicomimetic or para-sympathicolytic agent, a protein, a protein derivative, a psoriasis/neurodermatitis agent, a mydriatic agent, a mood elevator, a rhinological agent, a [sleeping draft] soporific, a [sleeping draft] soporific antagonist, a sedative, a spasmolytic, a tuberculosis agent, a urological agent, a vasoconstrictor, a vasodilator, a virostatic agent, a wound-healing agent, and a non-steroidal antiinflammatory agent.

85. The method of claim 53, wherein the active [ingredient] agent is a nonsteroidal anti-inflammatory drug selected from the group consisting of diclofenac, ibuprofin, and a lithium, sodium, potassium, cesium, rubidium, ammonium, monoethyl, dimethyl, trimethylammonium or ethylammonium salt thereof.

87. The method of claim 53, wherein the active [ingredient] agent is a growth regulating substance.

88. The method of claim 53, wherein the active [ingredient] agent is selected from the group consisting of an insecticide, a pesticide, a herbicide or a fungicide.

89. The method of claim 53, wherein the active [ingredient] agent is an allurement.